



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460



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MEMORANDUM

SUBJECT: Metabolism Study Review for PMN 08-508/509

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I. INTRODUCTION

Two Absorption, Distribution, Metabolism, Excretion (ADME) studies were submitted for PMN substances 08-508 and 509; the test substance in both studies was PMN substance 08-509 ([REDACTED]). One study was conducted in mice ([REDACTED]) and the other in rats ([REDACTED]).

PMN substance 08-508, 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid (CAS No.13252-13-6, Figure 1), is a [REDACTED] with a molecular weight of 330, a boiling point of [REDACTED] (PMN submission), an estimated water solubility of 43 mg/L, and an estimated log  $K_{ow}$  of 8.12 (SAT Report).

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PMN substance 08-509, 2,3,3,3 -tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt (CAS No. 62037-80-3, Figure 1), is a [REDACTED] with a molecular weight of 347, it is dispersible in water (PMN submission).

## II. REVIEW OF MOUSE STUDY

### A. Study Description

"The absorption, distribution, metabolism, and elimination of [REDACTED] were investigated in the Crl:CD1(ICR) mouse. [REDACTED] was administered in water to 5 male and 5 female mice as a single oral dose at a target dose level of 3 mg [REDACTED]/kg body weight (bw) and a dose volume of 10 mL/kg bw. Mice were housed individually in metabolism units and urine and feces were collected on dry ice predose and postdose at 0-6 hours, 6-12 hours, 12-24 hours, and every 24 hours until 168 hours post-dose. At 168 hours post-dose mice were asphyxiated by exposure to carbon dioxide and then sacrificed by exsanguination. The following tissues (Tier 1) were collected: liver; fat; G.I. tract (and contents); kidney; spleen; whole blood; residual carcass and stored at  $-10^{\circ}\text{C}$ . [REDACTED] was quantitated in urine, feces, and cage wash by liquid chromatography tandem mass spectrometry (LC/MS/MS). Urine samples were further evaluated by LC/MS to confirm the identity of the parent analyte and determine if [REDACTED] was eliminated metabolized or unmetabolized [REDACTED]."

### B. Results and Study Author's Conclusions

The following paragraphs are quoted from [REDACTED]

Following oral administration of [REDACTED] in water,  $30.8\% \pm 5.37\%$  and  $39.3\% \pm 5.58\%$  of the administered dose was accounted for in urine (0-12 hours) from male and female mice, respectively. At the conclusion of the study (168 hours post-dose), the total accumulated amount of [REDACTED] detected in urine was  $89.5\% \pm 6.91\%$  and  $91.5\% \pm 6.04\%$  of the administered dose for male and female mice, respectively.

Elimination of [REDACTED] via urine accounted for a majority of the administered dose for both male and female mice; minor levels of [REDACTED] detected in feces from male ( $2.00\% \pm 1.01\%$ ) and female mice ( $1.91\% \pm 0.85\%$ ) were likely contamination from urine.

[REDACTED]

Cage wash, which is composed of dried excreta (urine and feces), accounted for  $9.64\% \pm 3.99\%$  and  $6.25\% \pm 3.16\%$  of the administered dose for male and female mice, respectively. Following oral dosing with [REDACTED] in water and a 168 hour post-dose collection period,  $101.2\% \pm 3.22\%$  and  $99.7\% \pm 2.95\%$  of the administered dose was recovered from male and female mice, respectively.

Samples of urine evaluated using LC/MS were found to contain only the parent substance, [REDACTED]. This finding, taken with recovery of the administered dose in urine, confirms that [REDACTED] was rapidly absorbed and eliminated unmetabolized following oral dosing in the mouse.

### III. REVIEW OF RAT STUDY

#### A. Study Description

"The absorption, distribution, metabolism, and elimination of [REDACTED] were investigated in the Sprague-Dawley rat. [REDACTED] was administered in water to 5 male and 5 female rats as a single oral dose at a target dose level of 30 mg [REDACTED]/kg body weight (bw) and a dose volume of 4 mL/kg bw. Rats were housed individually in glass metabolism units and urine and feces were collected on dry ice predose and postdose at 0-6 hours, 6-12 hours, 12-24 hours, and every 24 hours until 168 hours post-dose. At 168 hours post-dose rats were asphyxiated by exposure to carbon dioxide and then sacrificed by exsanguination. The following tissues (Tier 1) were collected: liver; fat; G.I. tract (and contents); kidney; spleen; whole blood; residual carcass and stored at  $<-10$  deg C. [REDACTED] was quantitated in urine, feces, and cage wash by liquid chromatography tandem mass spectrometry (LC/MS/MS). Urine samples were further evaluated by LC/MS to confirm the identity of the parent analyte and determine if [REDACTED] was eliminated metabolized or unmetabolized (Fasano, 2010b)."

#### B. Results and Study Author's Conclusions

The following paragraphs are quoted from [REDACTED] [REDACTED]

[REDACTED]

Following oral administration of [REDACTED], in water,  $96.6\% \pm 1.43\%$  and  $94.6\% \pm 8.57\%$  of the administered dose was accounted for in urine (0-12 hours) from male and female rats, respectively. At the conclusion of the study (168 hours post-dose), the total accumulated amount of [REDACTED] detected in urine was  $103\% \pm 2.73\%$  and  $99.8\% \pm 6.41\%$  of the administered dose for male and female rats, respectively.

Elimination of [REDACTED] via urine was rapid and accounted for a majority of the administered dose for both male and female rats; negligible levels of [REDACTED] detected in feces from male ( $1.35\% \pm 1.05\%$ ) and female rats ( $0.85\% \pm 0.58\%$ ), were likely contamination from urine. Cage wash, which is composed of dried excreta (urine and feces), accounted for  $0.98\% \pm 0.52\%$  and  $5.03\% \pm 5.14\%$  of the administered dose for male and female rats, respectively.

Following oral dosing with [REDACTED] in water and a 168 hour post-dose collection period,  $105.3\% \pm 2.19\%$  and  $105.7\% \pm 1.42\%$  of the administered dose was recovered from male and female rats, respectively.

Samples of urine evaluated using LC/MS were found to contain only the parent substance, [REDACTED]. This finding, taken with the complete recovery of the administered dose in urine, confirms that [REDACTED] was rapidly absorbed and eliminated unmetabolized following oral dosing in the rat.

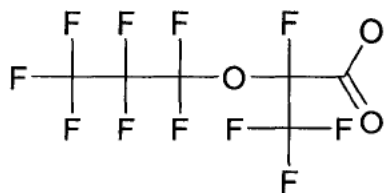
#### IV. REVIEWER'S CONCLUSIONS

This reviewer agrees that PMN substance 08-509 [REDACTED] is rapidly absorbed from the GI tract and rapidly excreted, primarily in the urine, in both rats and mice. Excretion does appear to be somewhat slower in the mouse (31 - 39% in 12 hours; 90 - 91% total over 168 hours) than in the rat (95 - 97% in 12 hours; ca. 100% total over 168 hours). The study was not designed to determine the half-life of excretion.

The only material excreted in the urine was PMN substance 08-509 [REDACTED].

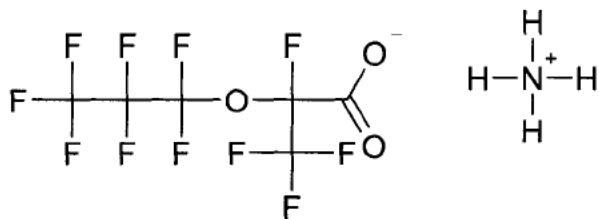
[REDACTED]

PMN Substance 08-508



2,3,3,3-Tetrafluoro-2-(heptafluoropropoxy)propionic acid

PMN Substance 08-509



2,3,3,3-Tetrafluoro-2-(heptafluoropropoxy)propionic acid,  
ammonium salt

Figure 1. Structures of PMN Substances 08-508 and 509.

# REFERENCES

[REDACTED] [REDACTED] [REDACTED] [REDACTED]). [REDACTED]: Absorption,  
Distribution, Metabolism, and Elimination in the Mouse. [REDACTED]  
[REDACTED] | Performed by: [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]

[REDACTED] [REDACTED] [REDACTED] [REDACTED]. [REDACTED] Absorption,  
Distribution, Metabolism, and Elimination in the Rat. [REDACTED]  
[REDACTED]. Performed by: [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]  
[REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED]

[REDACTED]